REMARKS

In the office action dated February 28, 2008, the Examiner notes that the amendment filed on 12/10/2007 was not incompliance with 37 CFR 1.121(c) because there are no claims 15-16 in the present claims. Claims 15 and 16 were inadvertently omitted from the amendment filed on November 19, 2007. Claims 15 and 16 have been inserted into this amendment.

I. The Pending Claims Are Not Anticipated By Chenchick et al., Bandaru et al., nor Wagner et al.

The present invention is directed to a high through-put system for analyzing gene expression. Using the invention, large numbers of antibodies are used to interrogate paired samples from human tissue to determine which genes are expressed or not expressed in different conditions. In one example, samples from normal and cancerous tissue are interrogated by 100, of antibodies to identify genes that are differentially expressed in cancer or, alternatively, expressed in normal tissue and not expressed in cancer. This we find is valuable for identifying diagnostic markers or for identifying genes and proteins that are potential therapeutic targets.

In the present invention, gene expression differences in paired samples (tissue or fluids) of human patients in different conditions, whether normal and disease or different stages of diseases, are correlated by reacting a large population of antibodies with the samples. In each case one antibody corresponds to one gene and one gene expression product and when the same matrix of samples is interrogated simultaneously by this plurality of antibodies, gene expression data for hundreds of genes is obtained in a high through-put fashion. Simultaneous gene expression data is generated for hundreds of genes because they are cumulated to a single antibody by virtue of the gene having been used to raise the antibody through in vivo immunization.

The normal and diseased (different biological conditions) from many different human samples, whether tissues or any biological fluids, from many different individuals for expression

analysis or diagnostic applications are analyzed. The biological samples and the population of antibodies are analyzed simultaneously on the same array.

In contrast, the specification of Chenchik provides an array of immobilized proteins arranged according to size which could be probed by several antibodies provided they differ in the binding even to one distinguished by the use of different labels as in an ordinary DNA array. Therefore, the same protein array could only be probed by a small number of antibodies, because only a little number of signal elements, Chenchik's different colored fluorophores, are available.

In contrast, in the claimed invention, a matrix of complex biological samples is spotted or associated to a solid support in a physical compartment, and this matrix is repeated several times in as many compartments as there are on the support, and each compartment is interrogated by one antibody from the population of 100 antibodies so that a plurality of proteins in the sample is interrogated by the antibodies simultaneously.

Neither the high through-put format nor the use of the number of antibodies corresponding to the number of expressed gene products is anticipated by Chenchik.

Chenchick does not contemplate the concept of repetitive compartmentalization of a matrix of proteins that can be interrogated by a number of antibodies simultaneously.

The Chenchick reference is a conventional example of a protein chip when the size of the member bound to the array assists in the identification of binding events. The so-called "probe" in the Chenchick disclosure is analogous to the binding antibodies of the present invention. However, Chenchick does not correlate specific antibodies used in the reaction to specific genes that may be subject to differential expression analysis. Thus, although Chenchick notes that the array described therein can be used for differential expression analysis, the differential expression does not extend to use at a population of antibodies where each is linked to a particular gene expression product and a particular gene.

Bandaru Does Not Disclose The Element of the Pending Claims Identified in the Previous Action.

The method of Bandaru relies on capture probes binding the sites on an array. The method of Bandaru do not use antibody binding events from an entire population of antibodies across an array for de novo expression profiling. Bandaru's only disclosure uses a novel thioredoxin to evaluate the presence in a sample (tissue, biopsy, or fluid sample) from a subject before and after treatment, i.e. in two different conditions, and compares the level of this novel thioredoxin polypeptide in these two conditions (see e.g. col. 4, lines 9-13, and col. 10, lines 21-55).

Bandaru also describes a possible use of his novel protein, gene, and corresponding antibody in the context of arrays (col. 49, col. 51). Bandaru does not disclose the use of antibodies across the array, the plurality of complex biological samples (i.e. before and after treatment), or the use of a large number of antibodies in a repetitive fashion with a matrix.

Wagner et al Does Not Anticipate the Presently Claimed Method

Although the Examiner states that:

1) "Wagner et al disclose a method of comparing the protein expression of two cells or a population of cells that have been exposed to different conditions (col. 37 lines 16-67)", and that

2) "the method of Wagner does perform the method step of containing two tissue samples onto an array to obtain gene expression analysis because Wagner et al. define an array as an arrangement of entities in a pattern on a substrate and the array have plurality of different protein-capture agents".

Wagner cannot analyze two protein-containing samples on the SAME antibody array at all. Wagner can only perform that method step on two separate antibody arrays containing the same antibodies, yet contacted or probed with two different samples. This has to be performed in parallel not simultaneously.

This is confirmed by the definition of "plurality" of protein binding partners (col. 11 line 57 col. 12 line 9): Wagner talks about a plurality of proteins or gene expression products yet from a single organism, or single tissue, or single organ.

Furthermore, Wagner et al. can not perform the method step of containing two tissue samples onto an array to obtain gene expression analysis, but instead rely on two samples using two identical arrays. Wagner et al. cannot perform the step wherein each member of the plurality of antibodies is identified as having specific binding affinity to an expression product of a gene sequence. . . ." Because this element is necessarily lacking from Wagner et al., Wagner et al. cannot anticipate under Section 102(a).

None of the above references meet the limitations of dependent claim 15 wherein antibodies are raised by in vivo immunization of a gene sequence. Applicants are specifically arguing the separate patentability of claim 15.

In light of the above, applicant requests favorable consideration and allowance of all of the newly presented claims. If the Examiner has any questions regarding the foregoing, or if the Examiner believes that an interview would facilitate the examination of this application, or if any additional information is required, the Examiner is invited to contact the undersigned at 949/567-6700, X 7740.

The Commissioner is authorized to charge a three month extension fee of $525.00 to ORRICK, HERRINGTON & SUTCLIFFE LLP's Deposit Account No. 150665. The Commissioner is also authorized to charge all applicable fees to ORRICK, HERRINGTON & SUTCLIFFE LLP's Deposit Account No. 150665 and to credit any overpayments to said Deposit Account No. 150665.

Respectfully submitted,

ORRICK, HERRINGTON & SUTCLIFFE LLP

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